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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,451	12/20/2001	Jesper Z. Haeggstrom	PVZ-006US	4167
959 7590 08/20/2007 LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER KIM, ALEXANDER D	
			ART UNIT 1656	PAPER NUMBER
			MAIL DATE 08/20/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/914,451

Applicant(s)

HAEGGSTROM ET AL.

Examiner

Alexander D. Kim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 60-77 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 60-77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

1. In response to the previous Office actions, a non-Final rejection (mailed on 06/20/2006), Applicants filed a response and amendment received on 12/22/2006 (mailing date of December 20th, 2001). Said amendment cancelled Claims 1-59; and added new Claims 60-77. Thus, Claims 60-77 are pending in the instant Office action.

Petition

2. Applicant's petition under 37 CFR 1.137(b) filed on 12/22/2006 to revive the instant application has been granted on 5/30/2007.

Priority

3. Examiner suggests that applicants update the status of the prior filed applications in the specification's continuing data at page 1 of the specification.

Withdrawn-Claim Rejections - 35 U.S.C. § 112, Second Paragraph

4. The previous rejection of Claims 36 and 38-59 under 35 U.S.C. § 112, second paragraph, is withdrawn by the virtue of Applicants' canceling all previous claims.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

5. Claims 70-77 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 70 recite the limitation "X-ray crystallography". The term is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus, x-ray crystallography is interpreted as a method having any steps involved in determining the coordinates of a crystal comprising crystallization, x-ray diffraction, computation, and phasing, for example. As it is written, it is unclear if the step requires the crystallization of claimed hydrolase. In light of specification examples, refining the crystallization condition in the presence of the hydrolase, the claims will be interpreted as having a step of crystallization with the claimed hydrolase for the examination purpose. Appropriate clarification is required.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

6. Claims 60-77 are rejected under 35 U.S.C. § 112, first paragraph, **written description**, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The rejection was stated in the previous office action as it applied to previous Claims 36 and 38-59. In response to this rejection, applicants have cancelled all claims and added new claims 60-77 and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. As noted above, the Claim 70 reciting "x-ray crystallography" is interpreted as a method having any steps involved in determining the coordinates of crystal comprising crystallization, x-ray diffraction, computation, and phasing, for example.

Applicants argue that Applicants were in possession of the claimed invention based on the teachings in the specification, the general knowledge in the art at the time of the filing and the example of active sites of the LTA4 hydrolase in page 12-14, which teaches a leukotriene binding site and a general catalytic domain for the M1 class of enzymes. Thus, Applicants further argue the functionally equivalent part is sufficiently described.

The instant claims are drawn to a method of identifying compounds or designing an inhibitor or agonist of any leukotriene A₄ hydrolase comprising: crystallizing any leukotriene A₄ hydrolase or use of cycles of X-ray crystallography, which also involves crystallizing any said enzyme and solving the structure for determining the three-dimensional coordinates, as disclosed in Claims 60 and 70. Claims 62-64 are drawn to a method comprises crystallizing said hydrolase with any "complexing agents" including thiolamine or hydroxamic acid. The claimed leukotriene A₄ hydrolase encompasses a very widely varying genus of enzyme includes, but not limited to, any leukotriene A₄

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hydrolase from any source, an enzyme having a functional equivalent of leukotriene A₄ hydrolase activity with unlimited structure or any enzyme having catalytic domain similar to leukotriene A₄ hydrolase. The interpretation of the claimed genus having unlimited structure is also supported by the instant Claims 65-67, 69, 73-75 and 77, which supposed to be further limiting from the independent Claim 60 or 70. Claims 65-67, 69, 73-75 and 77 encompasses method comprising said amino acid residues in Claim 66 but not limited to the amino acid in SEQ ID NO: 1 by the reasonable interpretation of recited term "set forth in" or "defined by" and Applicants' argument that instant claims would encompass M1 class of enzymes because of a common feature of general catalytic domain. Thus, any enzyme having those said amino acid residues and hydrolyze any parts of leukotriene A₄ molecule (including any functional equivalent) is encompassed by the instant claims. Applicants also argue the genus of compounds is sufficiently supported by the specification and the general knowledge in the art would appreciate the importance of said LTA₄ hydrolase in the pathogenesis (see bottom pf page 7, Remark).

As disclosed in the previous Office Action, page 7-8, "the instant specification discloses the full-set of structural coordinates of LTA₄H as set forth in Table 9, used in the claimed method. However, the instant specification does not disclose the structure coordinates of LTA₄H as directed to the "functional equivalent part thereof". "Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated protein three-dimensional model and compound possibilities recited in the instant claims. Consequently, conception in either case cannot be

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achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention". Furthermore, the instant claims 60-61 and 70-72 (reciting "crystallizing" and "X-ray crystallography", respectively) encompass a method of crystallizing the broad genus of claimed LTA4 hydrolase which can not be described by the instant disclosure or by prior arts. Claims 62-67, 69, 73-75 and 77 encompass a method comprising crystallizing enzyme having recited amino acid residues in claims but not limited to the specific amino acid residues in SEQ ID NO: 1 by the reasonable interpretation of recited term "set forth" or "defined by" and Applicants' argument that instant claims would encompass M1 class of enzymes because of a common feature of general catalytic domain. The Claims 60, 62 -64, 70 encompass a method comprising a crystallization of broad genus hydrolase in the presence any molecule including thiolamine or hydroxamic acid, wherein Applicants acknowledge the crystallizing a protein is not routine and is "a major difficulties" (see page 11, middle, Remarks) and the Applicants notes that the crystallization of instant example "were only obtained when the inhibitor bestatin was present in the crystallization set-ups" (see page 36, lines 11-12).

For the reasons above, the instant specification does not provide a sufficient structure/functional relationship for one skilled in the art to have possession of the full scope of the claimed invention. Thus, the instant rejection is maintained.

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7. Claims 66-70 are rejected under 35 U.S.C. § 112, first paragraph, **scope of enablement**, because the specification, while being enabling for a method comprising: crystallizing the use of structural coordinates of a human LTA₄ hydrolase protein, determining the coordinates disclosed in Table 9 and screening the set of candidate compound by said coordinates, does not reasonably provide enablement for a method comprising: crystallizing any LTA₄ hydrolase or any enzyme having leukotriene A₄ hydrolase activity (including a functional equivalent, homolog, for example) for structure determination and screening any molecules with unlimited structure limitation.

The rejection was stated in the previous office action as it applied to previous Claims 36 and 38-59. In response to this rejection, applicants have cancelled all claims and added new claims 60-77 and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. As noted above, the Claim 70 reciting "x-ray crystallography" is interpreted as a method having any steps involved in determining the coordinates of crystal comprising crystallization, x-ray diffraction, computation, and phasing, for example.

Applicants argue "one of ordinary skill in the art would be able to make and use the claimed invention using only routine experimentation" (see middle of page 8, Remarks) by the teachings in the specification and the general knowledge in the art, wherein the routine experimentation use the active site of the LTA₄ hydrolase. Thus, "one skilled in the art would be able to design functionally equivalent parts of the LTA₄ hydrolase" (see tope of page 9, Remarks). Applicants also argue "it would be routine

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for a skilled artisan to test the ability of identified and/or designed compounds that bind to LTA₄ hydrolase" (see top of page 9, Remarks).

However, as noted above, Applicants acknowledge making a high quality protein crystal is not routine and is "a major difficulties" (see page 11, middle, Remarks) and overcoming the phase problem render a skilled artisan doubtful of achieving the claimed invention (see page 11, bottom, Remarks). Furthermore, Applicants notes that the crystallization of instant example "were only obtained when the inhibitor bestatin was present in the crystallization set-ups" (see page 36, lines 11-12). Thus, the method of Claims 61-64 and 72 (reciting any other binding molecules) would require further complicate the experimentation(s) for crystallization of very broad said hydrolase, with or without any molecules for co-crystallization. Also, as noted in the previous Office Action, in order to identify, select, and design by studying the interaction of a species (i.e. compound) with a molecular structure of any LTA₄ hydrolase or any enzyme encompassed by the instant claims, one skilled in the art would require the three dimensional structure coordinates of all proteins thereof. Applicants have failed to provide guidance to obtain the atomic coordinates of all LTA₄ hydrolase protein encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Also, identifying a compound from unlimited species of compounds or synthesizing any compound require a further undue experimentation and one skilled in the art would require undue experimentation for a method of synthesizing any unlimited number of compound in the Claim 70. Thus, the

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specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate with the full scope of the claims.

For the reasons above and the previous Office Action, the instant scope of enablement rejection is maintained.

Claim Rejections - 35 U.S.C. § 103

8. The previous rejection of Claims 36, 38-41 and 43-59 under 35 U.S.C. § 103(a) as being unpatentable over Balaji *et al.* (US Patent 5,579,250, Balaji) in view *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Ngai* 70 USPQ2d 1862 (Fed. Cir. 2004) is withdrawn by the virtue of Applicants' amendment.

Conclusion

9. Claims 60-77 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim
August 3, 2007

A handwritten signature in black ink, appearing to read 'Richard Hutson', with a long horizontal line extending to the right.

RICHARD HUTSON, PH.D.
PRIMARY EXAMINER